

Claims

1. Use of inhibitors of dipeptidylpeptidase IV (DP IV) as well as of inhibitors of enzymes having a similar substrate specificity (DP IV-analogous enzyme activity) and/or of inhibitors of alanyl aminopeptidase (aminopeptidase N, APN) as well as of inhibitors of enzymes having a similar substrate specificity (APN-analogous enzyme activity) for the preparation of pharmaceutical preparations for the inhibition of the proliferation (DNA synthesis) of human sebaceous cells.
2. The use according to claim 1, wherein the inhibitors of DP IV are selected from Xaa-Pro-dipeptides (Xaa = α -amino acid or side-chain protected derivative), corresponding derivatives, preferably dipeptide phosphonic acid diaryl esters, dipeptide boronic acids (e. g. Pro-boro-Pro) and their salts, Xaa-Xaa-(Trp)-Pro-(Xaa)_n peptides (Xaa = α -amino acid, n = 0 to 10), corresponding derivatives and their salts, amino acid (Xaa) amides, corresponding derivatives and their salts, wherein Xaa is an α -amino acid or a side chain-protected derivative, preferably N^ε-4-nitrobenzyl oxycarbonyl-L-lysine, L-isoleucine, L-valine, L-tryptophane, L-proline, and cyclic amines as, for example, pyrrolidine, piperidine, thiazolidine and their derivatives act as the amide structure, tryptophane-1,2,3,4-tetrahydroisochinoline-3-carboxylic acid derivatives (TSL) and/or (2S,2S',2S'')-2-[2'-[2''-amino-3'''-(indol-3'''-yl)-1''-oxopropyl]-1',2',3',4'-tetrahydro-6'8'-dihydroxy-7-methoxyisochinol-3-yl-carbonyl-amino]-4-hydromethyl-5-hydropentanoic acid (TMC-2A).
3. The use according to claim 1, wherein amino acid amides are used as DP IV inhibitors, preferably N^ε-4-nitrobenzyl-oxycarbonyl-L-lysine thiazolidide, pyrrolidide and piperidide as well as the corresponding 2-cyano thiazolidide, 2-cyano pyrrolidide and 2-cyano piperidide derivative.
4. The use according to claim 1, wherein actinonin, leuhistin, phebestin, amastatin, bes-tatin, probestin, β -aminothiols, α -aminophosphinic acids, α -amino phosphinic acid de-

rivatives, preferably D- Phe- ψ -[PO(OH)-CH₂]-Phe-Phe, and their salts act as inhibitors of APN.

5. Use of inhibitor combinations according to any of the claims 1 to 4 for manufacturing pharmaceutical preparations for a prevention and therapy of both benign follicular hyperproliferation conditions (acne, acneiform follicular reactions, steatocystoma multiplex, naevi of sebaceous glands, senile sebaceous gland hypertrophy, seborrhea of the skin and of the hair), SAHA syndrome [seborrhea, acne, hirsutism, alopecia] and malign follicular hyperproliferation conditions (mixed tumors, sebaceomas, naevus sebaceus with malign development, sebaceous gland tumors, sebaceous gland CA).
6. Use of inhibitors of dipeptidylpeptidase IV (DP IV) as well as of inhibitors of enzymes having a similar substrate specificity (DP IV-analogous enzyme activity) and/or of inhibitors of alanyl aminopeptidase (aminopeptidase N, APN) as well as of inhibitors of enzymes having a similar substrate specificity (APN-analogous enzyme activity) for the inhibition of the proliferation (DNA synthesis) of human sebaceous cells.
7. Use according to claim 6, wherein the inhibitors of the DP IV are selected from Xaa-Pro-dipeptides (Xaa = α -amino acid or side-chain protected derivative), corresponding derivatives, preferably dipeptide phosphonic acid diaryl esters, dipeptide boronic acids (e. g. Pro-boro-Pro) and their salts, Xaa-Xaa-(Trp)-Pro-(Xaa)_n peptides (Xaa = α -amino acid, n = 0 to 10), corresponding derivatives and their salts, amino acid (Xaa) amides, corresponding derivatives and their salts, wherein Xaa is an α -amino acid or a side chain-protected derivative, preferably N^ε-4-nitrobenzyloxy carbonyl-L-lysine, L-isoleucine, L-valine, L-tryptophane, L-proline, and cyclic amines, for example pyrrolidine, piperidine, thiazolidine and their derivatives act as the amide structure, tryptophane-1,2,3,4-tetrahydroisochinoline-3-carboxylic acid derivatives (TSL) and/or (2S,2S',2S'')-2-[2'-[2''-amino-3''-(indol-3'''-yl)-1''-oxopropyl]-1',2',3',4'-tetrahydro-6'8'-dihydroxy-7-methoxyisochinol-3-yl-carbonyl-amino]-4-hydromethyl-5-hydropentanoic acid (TMC-2A).

8. Use according to claim 6, wherein amino acid amides are used as DP IV inhibitors, preferably N^ε-4-nitrobenzyl-oxycarbonyl-L-lysine thiazolidide, pyrrolidide and piperidide as well as the corresponding 2-cyano thiazolidide, 2-cyano pyrrolidide and 2-cyano piperidide derivative.
9. Use according to claim 6, wherein actinonin, leuhistin, phebestin, amastatin, bestatin, probestin, β-aminothiols, α-aminophosphinic acids, α-amino phosphinic acid derivatives, preferably D-Phe-ψ[PO(OH)-CH₂]-Phe-Phe, and their salts act as inhibitors of APN.
10. Use of inhibitor combinations according to any of the claims 6 to 9 for a prevention and therapy of both benign follicular hyperproliferation conditions (acne, acneiform follicular reactions, steatocystoma multiplex, naevi of sebaceous glands, senile sebaceous gland hypertrophy, seborrhea of the skin and of the hair), SAHA syndrome [seborrhea, acne, hirsutism, alopecia] and malign follicular hyperproliferation conditions (mixed tumors, sebaceomes, naevus sebaceus with malign development, sebaceous gland tumors, sebaceous gland CA).
11. A process for the inhibition of the proliferation (DNS synthesis) of human sebaceous cells (sebocytes) including the singular or the repeated administration of a pharmaceutical preparation to a patient with the corresponding disease pattern, comprising the administration of inhibitors of dipeptidylpeptidase IV (DP IV) as well as of inhibitors of enzymes having a similar substrate specificity (DP IV-analogous enzyme activity) and/or of inhibitors of alanyl aminopeptidase (aminopeptidase N, APN) as well as of inhibitors of enzymes having a similar substrate specificity (APN-analogous enzyme activity).
12. Process according to claim 11, wherein the inhibitors of the DP IV are selected from Xaa-Pro-dipeptides (Xaa = α-amino acid or side-chain protected derivative), corresponding derivatives, preferably dipeptide phosphonic acid diaryl esters, dipeptide boronic acids (e. g. Pro-boro-Pro) and their salts, Xaa-Xaa-(Trp)-Pro-(Xaa)_n peptides

(Xaa = α -amino acid, n = 0 to 10), corresponding derivatives and their salts, amino acid (Xaa) amides, corresponding derivatives and their salts, wherein Xaa is an α -amino acid or a side chain-protected derivative, preferably N^ε-4-nitrobenzyloxy carbonyl-L-lysine, L-isoleucine, L-valine, L-tryptophane, L-pro-line, and cyclic amines, for example pyrrolidine, piperidine, thiazolidine and their derivatives act as the amide structure, tryptophane-1,2,3,4-tetrahydroisochinoline-3-carboxylic acid derivatives (TSL) and/or (2S,2S',2S'')-2-[2'-[2''-amino-3'''-(indol-3'''-yl)-1''-oxopropyl]-1',2',3',4'-tetrahydro-6'8'-dihydroxy-7-methoxyisochinol-3-yl-carbonyl-amino]-4-hydromethyl-5-hydropentanoic acid (TMC-2A).

13. Process according to claim 11, wherein amino acid amides are used as DP IV inhibitors, preferably N^ε-4-nitrobenzyl-oxycarbonyl-L-lysine thiazolidide, pyrrolidide and piperidide as well as the corresponding 2-cyano thiazolidide, 2-cyano pyrrolidide and 2-cyano piperidide derivative.
14. Process according to claim 11, wherein actinonin, leuhistin, phebestin, amastatin, bes-tatin, probestin, β -aminothiols, α -aminophosphinic acids, α -amino phosphinic acid de-derivatives, preferably D-Phe- ψ [PO(OH)-CH₂]-Phe-Phe, and their salts act as inhibitors of APN.
15. Process according to any of claims 11 to 14, for the prevention and therapy of both benign follicular hyperproliferation conditions (acne, acneiform follicular reactions, steatocystoma multiplex, naevi of sebaceous glands, senile sebaceous gland hypertro-phy, seborrhea of the skin and of the hair, SAHA-syndrom [seborrhoe, acne, hirsutism, alopecia]) and malign hyperproliferation conditions (mixed tumors, sebaceomes, naevus sebaceus with malign development, sebaceous gland tumors, sebaceous gland CA) on patients including the singular or the repeated administration of a pharmaceuti-cal preparation with one or more inhibitor(s) of DP IV and/or APN.
16. Pharmaceutical preparations, comprising inhibitors of dipeptidylpeptidase IV (DP IV) as well as of inhibitors of enzymes having a similar substrate specificity (DP IV-

analogous enzyme activity) and/or of inhibitors of alanyl aminopeptidase (aminopeptidase N, APN) as well as of inhibitors of enzymes having a similar substrate specificity (APN-analogous enzyme activity) in combination with per se known carrier substances, additives and/or auxiliary substances.

17. Pharmaceutical preparation according to claim 16, comprising Xaa-Pro-dipeptides (Xaa = α -amino acid or side-chain protected derivatives), corresponding derivatives, preferably dipeptide phosphonic acid diaryl esters and their salts, Xaa-Xaa-(Trp)-Pro-(Xaa)_n peptides (Xaa = α -amino acid, n = 0 to 10), corresponding derivatives and their salts, amino acid (Xaa) amides, corresponding derivatives and their salts, wherein Xaa is an α -amino acid or a side chain-protected derivative, preferably N^ε-4-nitrobenzyl-oxycarbonyl-L-lysine, L-isoleucine, L-valine, L-tryptophane, L-proline, and cyclic amines, for example pyrrolidine, piperidine, thiazolidine and their derivatives act as the amide structure, tryptophane-1,2,3,4-tetrahydroisochinoline-3-carboxylic acid derivatives (TSL) and/or (2S,2S',2S'')-2-[2'-[2''-amino-3'''-(indol-3'''-yl)-1''-oxopropyl]-1',2',3',4'-tetrahydro-6'8'-dihydroxy-7-methoxyisochinol-3-yl-carbonyl-amino]-4-hydromethyl-5-hydropentanoic acid (TMC-2A) as the inhibitors of the DP IV.
18. Pharmaceutical preparation according to claim 16, comprising amino acid amides, e.g. N^ε-4-nitrobenzyl-oxycarbonyl-L-lysine thiazolidide, pyrrolidide and piperidide as well as the corresponding 2-cyano thiazolidide, 2-cyano pyrrolidide and 2-cyano piperidide derivative as the inhibitors of the DP IV.
19. Pharmaceutical preparation according to claim 16, comprising actinonin, leuhistin, phebestin, amastatin, bestatin, probestin, β -aminothiols, α -aminophosphinic acids, α -amino phosphinic acid derivatives, preferably D-Phe- ψ [PO(OH)-CH₂]-Phe-Phe, and their salts as inhibitors of the APN.
20. Pharmaceutical preparation according to any of claims 16 to 19, comprising two or more of the inhibitors of DP IV or inhibitors of enzymes having a DP IV-analogous enzyme activity and/or inhibitors of APN or inhibitors of enzymes having an APN-

analogous enzyme activity, in a spaced-apart formulation in combination with per se known carrier substances, additives and/or auxiliary substances for a simultaneous or, with respect to time, immediately successive administration with the aim of a joint effect.

21. Pharmaceutical preparation according to any of claims 16 to 20 for a systemic administration for an oral, transdermal, intravenous, subcutaneous, intracutaneous, intramuscular, rectal, vaginal, sublingual application together with per se known carrier substances, additives and/or auxiliary substances.
22. Pharmaceutical preparation according to any of claims 16 to 20 for a topical administration in the form of cremes, ointments, pastes, gels, solutions, sprays, liposomes or nansomes, agitated mixtures, hydrocolloid dressings, and other dermatological bases/vehicles including instillative application.